## (19) World Intellectual Property Organization International Bureau





## (43) International Publication Date 23 May 2002 (23.05.2002)

### **PCT**

# (10) International Publication Number WO 02/040665 A3

(51) International Patent Classification<sup>7</sup>: 15/86, 7/01, 7/02

C12N 15/10,

(21) International Application Number: PCT/NL01/00824

(22) International Filing Date:

14 November 2001 (14.11.2001)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

09/713,678

15 November 2000 (15.11.2000) U

(71) Applicant (for all designated States except US): CRU-CELL HOLLAND B.V. [NL/NL]; Archimedesweg 4, NL-2333 CN Leiden (NL).

(72) Inventors; and

(75) Inventors/Applicants (for US only): VOGELS, Ronald [NL/NL]; Van Rietlaan 4, NL-3461 HW Linschoten (NL). HAVENGA, Menzo, Jans, Emco [NL/NL]; Wilhelmina Druckerstraat 66, NL-2401 KG Alphen a/d Rijn (NL). MEHTALI, Majid [FR/FR]; 12, rue General Leclerc, F-67115 Plobsheim (FR).

(74) Agent: PRINS, A., W.; c/o Vereenigde, Nieuwe Parklaan 97, NL-2587 BN The Hague (NL).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### Published:

with international search report

(88) Date of publication of the international search report:

17 October 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COMPLEMENTING CELL LINES

(57) Abstract: A packaging cell line capable of complementing recombinant adenoviruses based on serotypes from subgroup B, preferably adenovirus type 35. The cell line is preferably derived from primary, diploid human cells (e.g., primary human retinoblasts, primary human embryonic kidney cells and primary human amniocytes) which are transformed by adenovirus E1 sequences. Also disclosed is a cell line derived from PER.C6 (ECACC deposit number 96022940), which cell expresses functional Ad35 E1B sequences. The new cell lines are useful for producing recombinant adenoviruses designed for gene therapy and vaccination. The cell lines can also be used for producing human recombinant therapeutic proteins. In addition, the cell lines are useful for producing human viruses other than adenovirus such as influenza virus, herpes simplex virus, rotavirus, measles virus.



#### INTERNATIONAL SEARCH REPORT

Internation plication No PCT/NL 01/00824

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N15/10 C12N15/86 C12N7/01 C12N7/02 According to International Patent Classification (IPC) or to both national classification and IPC Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, BIOSIS C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. X DE 199 18 023 A (CICHON GUENTER) 1-17, 21 September 2000 (2000-09-21) 19-21. 33-42 the whole document X WO 99 32647 A (INTROGENE BV :SCHOUTEN 1-17,19GOVERT (NL); EINERHAND MARCUS PETER 20,33-42 WILHELM) 1 July 1999 (1999-07-01) abstract page 3, line 14 -page 7, line 23 page 21, line 10 - line 13 X DE 197 54 103 A (HEPAVEC AG FUER 1-17GENTHERAPIE) 10 June 1999 (1999-06-10) 19-21, 33-42 the whole document -/--Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) 'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "O" document referring to an oral disclosure, use, exhibition or other means \*P\* document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 4 July 2002 19/07/2002 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Panzica, G Fax: (+31-70) 340-3016

## INTERNATIONAL SEARCH REPORT

Internation! pilication No PCT/NL 01/00824

	PC1/NL 01/00824			
	15			
Citation of document, with Indication, where appropriate, of the relevant passages	Relevant to claim No.			
DE 198 07 265 A (CENTEON PHARMA GMBH) 26 August 1999 (1999-08-26) abstract column 4, line 16 - line 37	1-17,19, 20,33-42			
WO 98 17783 A (UNIV MICHIGAN)	1,3,5-11			
the whole document	2,4, 12-42			
WO 97 00326 A (FALLAUX FRITS JACOBUS ;UNIV LEIDEN (NL); BOUT ABRAHAM (NL); EB ALE) 3 January 1997 (1997-01-03) abstract page 3, line 16 - line 24 page 10, line 29 -page 11, line 14 page 18, line 25 -page 19, line 19 examples claims	1-17,19, 20,33-42			
US 5 880 102 A (BLAZING MICHAEL A ET AL) 9 March 1999 (1999-03-09) abstract examples	1-42			
SCHIEDNER G ET AL: "EFFICIENT TRANSFORMATION OF PRIMARY HUMAN AMNIOCYTES BY E1 FUNCTIONS OF AD5: GENERATION OF NEW CELL LINES FOR ADENOVIRAL VECTOR PRODUCTION" HUMAN GENE THERAPY, XX, XX, vol. 11, no. 15, 10 October 2000 (2000-10-10), pages 2105-2116, XP000974022 ISSN: 1043-0342 the whole document	1-17, 19-21, 33-42			
RUMPF H ET AL: "Two domains within the adenovirus type 12 E1A unique spacer have disparate effects on the interaction of E1A with P105- Rb and the transformation of primary mouse cells" VIROLOGY, ACADEMIC PRESS,ORLANDO, US, vol. 257, no. 1, 25 April 1999 (1999-04-25), pages 45-53, XP002134555 ISSN: 0042-6822 the whole document	1-42			
	DE 198 07 265 A (CENTEON PHARMA GMBH) 26 August 1999 (1999-08-26) abstract column 4, line 16 - line 37 W0 98 17783 A (UNIV MICHIGAN) 30 April 1998 (1998-04-30) the whole document  W0 97 00326 A (FALLAUX FRITS JACOBUS ;UNIV LEIDEN (NL); BOUT ABRAHAM (NL); EB ALE) 3 January 1997 (1997-01-03) abstract page 3, line 16 - line 24 page 10, line 29 -page 11, line 14 page 18, line 25 -page 19, line 19 examples claims  US 5 880 102 A (BLAZING MICHAEL A ET AL) 9 March 1999 (1999-03-09) abstract examples SCHIEDNER G ET AL: "EFFICIENT TRANSFORMATION OF PRIMARY HUMAN AMNIOCYTES BY E1 FUNCTIONS OF AD5: GENERATION OF NEW CELL LINES FOR ADENOVIRAL VECTOR PRODUCTION" HUMAN GENE THERAPY, XX, XX, vol. 11, no. 15, 10 October 2000 (2000-10-10), pages 2105-2116, XP000974022 ISSN: 1043-0342 the whole document  RUMPF H ET AL: "Two domains within the adenovirus type 12 E1A unique spacer have disparate effects on the interaction of E1A with P105- Rb and the transformation of primary mouse cells" VIROLOGY, ACADEMIC PRESS,ORLANDO, US, vol. 257, no. 1, 25 April 1999 (1999-04-25), pages 45-53, XP002134555 ISSN: 0042-6822			

# INTERNATIONAL SEARCH REPORT Infor ...... on patent family members

Internation Ilication No
PCT/NL 01/00824

			PCI/NL 01/00824			
Patent document cited in search report		Publication date		Patent family member(s)		Publication date
DE 19918023	Α	21-09-2000	DE	19918023	A1	21-09-2000
√WO 9932647	Α	01-07-1999	AU	1787499		12-07-1999
			CA	2316414		01-07-1999
			EP	1042494	A1	11-10-2000
		•	JP	2001526900		25-12-2001
			WO	9932647	A1	01-07-1999
DE 19754103	A	10-06-1999	DE	19754103	A1	10-06-1999
DE 19807265	Α	26-08-1999	DE	19807265		26-08-1999
			AU	1737899		02-09-1999
			EP	0950713		20-10-1999
			JP	11285394	A	19-10-1999
WO 9817783	Α	30-04-1998	US	5994132		30-11-1999
			AU	5152998		15-05-1998
			EP	0935648		18-08-1999
			WO	9817783		30-04-1998
			US	6063622		16-05-2000
			US	6083750		04-07-2000
			US	6057158	A 	02-05-2000
√WO 9700326	A	03-01-1997	AU	731767		05-04-2001
			AU	6018296		15-01-1997
			CA	2222140		03-01-1997
			EP	0833934		08-04-1998
			JP	11507552		06-07-1999
			MO	9700326		03-01-1997
			US		B1	28-05-2002
			US	6306652		23-10-2001
			US	6238893		29-05-2001.
			US	6265212		24-07-2001
			US	5994128		30-11-1999
			US 	6033908	A 	07-03-2000
US 5880102	Α	09-03-1999	NONE			